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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,094	02/26/2004	Susumu Ikehara	Q79949	4252

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/786,094	IKEHARA ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1 and 3-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1 and 3-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20070530* .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 11, 2007 has been entered. Claims 1, 3-14 have been amended. Claim 2 has been canceled. Claims 1 and 3-14 are pending and under consideration.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10 recite "HLA type as the host". The "host" as an individual entity lacks adequate antecedent basis within the claim. Amendment of sections (II) and (iii) of claim 1, claim 6-10 and 12-14 to recite "patient" in place of "host" would overcome this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or

guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 12 is drawn to a pharmacological composition for use in the method of claim 1 comprising (1)a composition containing donor-derived PBMC; (2) a composition containing PBMC derived from the patient or , or derived from a HLA-identical individual, and (3) a composition containing whole bone marrow cells derived from the patient or derived from a HLA-identical individual. Claim 14 is drawn to a pharmacological composition for use in claim 13 comprising (1) a composition containing PBMC derived from the patient or , or derived from a HLA-identical individual, and (2) a composition containing whole bone marrow cells derived from the patient or derived from a HLA-identical individual.

The instant specification teaches the individual use of the donor derived PBMC before the administration of either PBMC derived from the patient or derived from a HLA-identical individual, and whole bone marrow cells derived from the patient or derived from a HLA-identical individual (page 28, lines 6-11 and page 28, lines 19-24). Further, the specification teaches that PBMC derived from the patient or derived from a HLA-identical individual, is administered as a separate agent within 24 hours of administration of whole bone marrow cells derived from the patient or derived from a HLA-identical individual (page 29, lines 1-5). The specification provides no teachings as to how to use a pharmacological composition comprising both of PBMC derived from the patient or , or derived from a HLA-identical individual, and whole bone marrow cells derived from the patient or derived from a HLA-identical individual together. Further, the specification provides no teachings as how to use a pharmacological composition including the donor derived PBMC as a third ingredient. One of skill in the art would be subject to undue experimentation in order to use the claimed compositions comprising the three components of claim 12 and compositions comprising the two components of claim 14.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Matthes-Martin et al (Bone Marrow Transplantation, 2000, vol. 26, pp. 377-382) in view of Carella et al (Bone Marrow Transplantation, 2000, Vol. 25, pp. 345-350, reference of the IDS filed May 20, 2004).

Claim 10 is drawn in part to a method for the treatment of a malignant tumor comprising administering DLI to a patient having a malignant tumor; irradiation said patient and administering peripheral blood stem cells derived form the patient or peripheral blood stem cells which are HLA-identical to said patient.

Matthes-Martin et al teach allogenic stem cell transplantation as a method of treating juvenile myelomonocytic leukemia (abstract, first sentence). Matthes-Martin et al teach total body irradiation (TBI) as a method of pre-transplant conditioning and also teach that TBI does not have a significant impact on treatment-related mortality (page 381, first column, lines 13-17). Matthes-Martin et al teach that one patient received donor lymphocyte infusion followed by a 2nd bone marrow transplant (page 381, text immediately underneath Table 7). Matthes-Martin et al teach bone marrow as a source of stem cells for hematopoietic transplantation. Matthes-Martin et al do not teach peripheral blood as a source of stem cells for hematopoietic transplantation.

Carella et al teach stem cell transplantation by a donor lymphocyte infusion (DLI) containing mobilized blood stem cells (page 346, second column, lines 3-5 under the heading of "Focusing on immunosuppressive therapy pre-transplantation").

It would have been prima facie obvious at the time the claimed invention was made to substitute a DLI comprising mobilized blood stem cells in place of the bone marrow transplant used in the method of Matthes-Martin et al for treatment of all the patients, including the patient who required a second transplant after DLI. One of skill in the art would have been motivated to do so by the teachings of Carella et al on using mobilized blood stem cells in a DLI as a source of stem cells in an allograft and also because it easier to obtain HLA-identical stem cells from mobilized blood stem cells from peripheral blood rather than obtaining bone marrow which requires special procedures for removal from a donor. It would have been obvious to use total

body irradiation (TBI) as a means of conditioning before the stem cell transplant because Matthes-Martin et al teach that TBI does not have a significant impact on treatment-related mortality (TRM).

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roush et al (Transfusion Medicine Reviews, 2002, Vol. 16, pp. 161-176), the abstract of Ballester et al (Blood, vol. 100, no, 11, abstract no. 5198) and Ikehara et al (U.S. 6,383,481).

Claim 10 is drawn in part to a method for the prevention and treatment of graft vs host disease induced by donor lymphocyte infusion in a patient comprising administering DLI to a patient having a malignant tumor; irradiation said patient and administering peripheral blood stem cells derived form the patient or peripheral blood stem cells which are HLA-identical to said patient.

Roush et al teach donor lymphocyte infusion (DLI) therapy after stem cell transplantation. Roush et al teach that although disease remission has been attributed to DIL, the risk of graft vs. host disease may prevent the ultimate usefulness of said treatment (abstract and pages 167-169 under the heading "Complications of Donor Lymphocyte Infusion therapy")..

The abstract of Ballester et al teaches that a brief and intense period of graft vs host disease is desirable as it is correlated with a clinical beneficial graft vs myeloma effect. The abstract teaches the stem cell transplantation followed by DLI therapy using HLA-matched donors.

Ikchara et al teach that bone marrow transplantation has been subsumed to the expanded concept of hematopoietic stem cell transplantation (column 1, lines 26-27), and that the disclosed invention is a novel method of transplanting hematopoietic stem cells which overcomes the long-standing problems associated with stem cell transplantation, in particular the problem of graft failure and/or rejection (column 1, lines 55-59). Ikchara et al teach that the trend of allo-BMT using unrelated donor bone marrow has resulted in an increase of graft vs host disease and graft failure and/or rejection (column 1, lines 50-54). Ikchara et al teach that hematopoietic stem cells include mobilized peripheral blood stem cells (column 2, lines 30-33) and that

administration of said PBSC via the portal vein after total body irradiation (column 3, lines 5-13 and lines 48-67).

It would have been prima facie obvious at the time the claimed invention was made to follow the method of Roush et al using stem cell transplantation and DLI to induce disease remission with the method of Ikchara et al to induce tolerance to the HLA-identical stem cells mobilized from the peripheral blood. One of skill in the art would have been motivated to do so by the teachings of the abstract of Ballester et al on the necessity for a brief period of gvhd in order to attain clinical benefit and the teachings of Ikchara et al on how to attain immuno-tolerance to transplanted hematopoietic stem cells. One of skill in the art would have been motivated to use mobilized peripheral blood stem cell in place of bone marrow because it easier to obtain peripheral blood from a HLA-identical individual rather than bone marrow which requires special procedures for removal from a donor.

Claims 1, 4, 6-9, 11 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over Roush et al (Transfusion Medicine Reviews, 2002, Vol. 16, pp. 161-176) in view of the abstract of Ballester et al (Blood, vol. 100, no, 11, abstract no. 5198), Carella et al (Bone Marrow Transplantation, 2000, Vol. 25, pp. 345-350), Ikehara et al (U.S. 6,383,481) and Kushida et al (Blood, 2001, Vol. 97, pp. 3292-3299)..

Roush et al teach donor lymphocyte infusion (DLI) therapy after stem cell transplantation. Roush et al teach that although disease remission has been attributed to DIL, the risk of graft vs. host disease may prevent the ultimate usefulness of said treatment (abstract and pages 167-169 under the heading "Complications of Donor Lymphocyte Infusion therapy") Roush et al do not teach the specifics of how to overcome the problem of graft vs host disease after DLI treatment, or the specific type of stem cell transplant.

The abstract of Ballester et al teaches that a brief and intense period of graft vs host disease is desirable as it is correlated with a clinical beneficial graft vs myeloma effect. The abstract teaches the stem cell transplantation followed by DLI therapy using HLA-matched donors.

Carella et al teach stem cell transplantation by a donor lymphocyte infusion (DLI) containing mobilized blood stem cells (page 346, second column, lines 3-5 under the heading of "Focusing on immunosuppressive therapy pre-transplantation")

Ikchara et al teach that bone marrow transplantation has been subsumed to the expanded concept of hematopoietic stem cell transplantation (column 1, lines 26-27), and that the disclosed invention is a novel method of transplanting hematopoietic stem cells which overcomes the long-standing problems associated with stem cell transplantation, in particular the problem of graft failure and/or rejection (column 1, lines 55-59). Ikchara et al teach that the trend of allo-BMT using unrelated donor bone marrow has resulted in an increase of graft vs host disease and graft failure and/or rejection (column 1, lines 50-54). Ikchara et al teach that the hematopoietic stem cells include mobilized peripheral blood stem cells and bone marrow (column 2, lines 29-33) and that administration of said PBSC via the portal vein was carried out after total body irradiation (column 3, lines 5-13 and lines 48-67).

Kushida et al teach improvements to the method of Ikchara et al based on injection of BM cells directly into the bone rather than the portal vein and/or i.v. injection because the donor stromal cells provided to the bone marrow allow for proliferation and differentiation of donor hematopoietic stem cells and avoid the necessity of a laparoscopic procedure and an additional i.v. injection (pages 3292-3293, bridging paragraph)..

It would have been prima facie obvious at the time the claimed invention was made to follow the method of Roush et al using stem cell transplantation and DLI to induce disease remission with graft vs host disease and subsequently use the method of Kushida et al to induce tolerance to the HLA-identical stem cells in the context of a donor lymphocyte infusion as taught by Carella et al. One of skill in the art would have been motivated to do so by the teachings of the abstract of Ballester et al on the necessity for a brief period of gvhd in order to attain clinical benefit and the teachings of Ikchara et al on how to attain immuno-tolerance to transplanted hematopoietic stem cells after irradiation, and the improvement on the method of Ikchara et al as taught by Kushida et al. One of skill in the art would have been motivated to carry out a procedure using a single bone marrow injection in place of the procedure of Ikchara et al requiring a laparoscopic procedure and an i.v. injection in order to minimize the number of

procedures the patient was subjected to. One of skill in the art would have been motivated to provide a lymphocyte infusion from the same HLA-identical party who provided the bone marrow cells so that immune cells not originating from the bone marrow, such as T-cells, would be part of the reconstituted HLA-identical immune system.

Claims 1, 3, 4, 6-9, 11 and 13 rejected under 35 U.S.C. 103(a) as being unpatentable over Roush et al, the abstract of Ballester et al, Carella et al, Ikehara et al as applied to claims 1, 4, 6-9, 11 and 13 above, and further in view of Matthes-Martin et al (Bone Marrow Transplantation, 2000, vol. 26, pp. 377-382).

Claim 3 embodies the method f claim 1 wherein a first radiation is performed on the patient prior to the administration of DLI.

The combination of Roush et al, the abstract of Ballester, Carella et al and Ikchara et al does not specifically teach that the conditioning regimen before the initial stem cell transplantation and DLI was total body irradiation.

Matthes-Martin et al teach total body irradiation (TBI) as a method of pre-transplant conditioning and also teach that TBI does not have a significant impact on treatment-related mortality (page 381, first column, lines 13-17).

It would have been prima facie obvious at the time that the claimed invention was made to use TBI as pre-transplant conditioning before the first stem cell transplant and subsequent DLI. One of skill in the art would have been motivated to do so by the teachings of Matthes-Martin et al regarding lack of treatment-related mortality associated with total body irradiation as pre-transplant conditioning.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 4, 6-9, 11 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 4, 5 and 10 of copending Application No. 09/531,891 in view of Roush et al (Transfusion Medicine Reviews, 2002, Vol. 16, pp. 161-176), Carella et al (Bone Marrow Transplantation, 2000, Vol. 25, pp. 345-350, reference of the IDS filed May 20, 2004)and the abstract of Ballester et al (Blood, vol. 100, no, 11, abstract no. 5198).

The instant claims are drawn in part to a method of treating or preventing Graft vs Host Disease induced by donor lymphocyte infusion into a patient by irradiating said patient, infusing lymphocytes derived from a third party of identical HLA type or the host and providing intra-bone marrow transplantation using bone marrow cells derived from a third party of identical HLA type or the host.

Claim 10 of the '891 application is drawn in part to a method of inducing immunological tolerance in a patient undergoing bone marrow transplantation in whom an induction of immunological tolerance is needed comprising subjecting the patient to irradiation and administering to said irradiated patient an intra-bone marrow injection comprising an effective

amount of whole bone marrow cells and a pharmaceutical carrier. Claim 5 specifies that the method is for use in bone marrow transplantation. The claims of the '891 application do not specify that the immunological tolerance is to suppress graft versus host disease, or that a donor lymphocyte infusion is to be administered in addition to the intra-bone marrow injection. The claims of the '891 application do not require that the whole bone marrow cells be from the host or an HLA-identical donor. The claims of the '891 application do not provide for a first radiation treatment prior to the donor lymphocyte infusion of part A of claim 1.

Roush et al teach donor lymphocyte infusion (DLI) therapy after stem cell transplantation and after a exposure of a patient to radiation. Roush et al teach that although disease remission has been attributed to DIL, the risk of graft vs. host disease may prevent the ultimate usefulness of said treatment. Roush et al teach DIL from HLA-identical individuals.

Carella et al teach that DLI are necessary to convert the patient from hematopoietic mixed chimerism to full chimerism with the donor hematopoietic cells (Figure 1) and that this conversion allows for subsequent graft versus leukemia reactions along with graft versus host reactions.

The abstract of Ballester et al teaches that a brief and intense period of graft vs host disease is desirable as it is correlated with a clinical beneficial graft vs myeloma effect. The abstract teaches the stem cell transplantation followed by DLI therapy using HLA-matched donors.

It would have been prima facie obvious to carry out the methods of claims 3, 4, 5 and 10 of copending Application No. 09/531,891 in the manner of Roush et al for the purpose of inducing tolerance by means of a IBM-BMT matched with a lymphocyte infusion. One of skill in the art would have been motivated to do so by the teachings of Roush et al and Carella et al linking stem cell transplantation followed by DLI with both graft vs target cell and graft vs host reactions, the teachings of the abstract of Ballester et al on the necessity of an initial period of graft vs host disease in combination with graft vs target cell disease in order to obtain a clinical benefit against the target cell disease and the teachings of Carella et al on the necessity of DLI for the conversion to full chimerism with respect to grafted donor hematopoietic stem cells. One of skill in the art would have been motivated to combine the method of claims 3, 4, 5 and 10

of copending Application No. 09/531,891 with an infusion of HLA identical lymphocytes in order to have complete chimerism with the HLA-identical bone marrow cells.

This is a provisional obviousness-type double patenting rejection.

Claim 10 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,383,481 in view of Roush et al (Transfusion Medicine Reviews, 2002, Vol. 16, pp. 161-176), the abstract of Ballester et al (Blood, vol. 100, no, 11, abstract no. 5198) and Sherer and Shoenfeld (Bone Marrow Transplantation, 1998, Vol. 22, pp. 873-881).

Claim 10 is drawn in part to a method for the prevention and treatment of graft vs host disease induced by donor lymphocyte infusion in a patient comprising administering DLI to a patient having a malignant tumor; irradiation said patient and administering peripheral blood stem cells derived form the patient or peripheral blood stem cells which are HLA-identical to said patient.

Claims 1 and 2 of the '481 patent are drawn to a method of transplanting hematopoietic stem cells in a patient afflicted with autoimmune disease comprising subjecting the patient to radiation treatment that is lethal to said patients bone marrow cells, transplanting hematopoietic stem cells from a donor to the patient by portal vein administration, and transplanting hematopoietic stem cells from a donor to the patient by intravenous administration. The '481 patent defines hematopoietic stem cells as including mobilized peripheral blood stem cells (column 2, lines 30-34).

Sherer and Shoenfeld teach that autoimmune disease may be cured by allo-BMT in the same was as a hematological malignancy is eliminated by allo-BMT (page 873, second column, lines 23-26). Sherer and Shoenfeld teach that GVHD mimics autoimmune disease both pathogenically and clinically (page 878, second column, lines 2-4 of the final paragraph).

Roush et al teach donor lymphocyte infusion (DLI) therapy after stem cell transplantation and after a exposure of a patient to radiation. Roush et al teach that although disease remission

has been attributed to DIL, the risk of graft vs. host disease may prevent the ultimate usefulness of said treatment. Roush et al teach DIL from HLA-identical individuals.

The abstract of Ballester et al teaches that a brief and intense period of graft vs host disease is desirable as it is correlated with a clinical beneficial graft vs myeloma effect. The abstract teaches the stem cell transplantation followed by DLI therapy using HLA-matched donors.

Ikchara et al teach that bone marrow transplantation has been subsumed to the expanded concept of hematopoietic stem cell transplantation (column 1, lines 26-27), and that the disclosed invention is a novel method of transplanting hematopoietic stem cells which overcomes the long-standing problems associated with stem cell transplantation, in particular the problem of graft failure and/or rejection (column 1, lines 55-59). Ikchara et al teach that the trend of allo-BMT using unrelated donor bone marrow has resulted in an increase of graft vs host disease and graft failure and/or rejection (column 1, lines 50-54). Ikchara et al teach that the hematopoietic stem cells include mobilized peripheral blood stem cells (column 2, lines 30-33) and that administration of said PBSC via the portal vein after total body irradiation (column 3, lines 5-13 and lines 48-67).

It would have been prima facie obvious at the time the claimed invention was made to follow the method of Roush et al using stem cell transplantation and DLI to induce disease remission with the method of Ikchara et al to induce tolerance to the HLA-identical stem cells mobilized from the peripheral blood. One of skill in the art would have been motivated to do so by the teachings of the abstract of Ballester et al on the necessity for a brief period of gvhd in order to attain clinical benefit and the teachings of Ikchara et al on how to attain immuno-tolerance to transplanted hematopoietic stem cells. One of skill in the art would have been motivated to use mobilized peripheral blood stem cell in place of bone marrow because it easier to obtain peripheral blood from a HLA-identical individual rather than bone marrow which requires special procedures for removal from a donor.

All other rejections and objections as set forth or maintained in the previous Office action are withdrawn in.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A. Canella/
Ph.D., Primary Examiner
Art Unit 1643